

Minerva Neurosciences Announces Study Results Demonstrating Bioequivalence of Phase 2b, Phase 3, and Planned Commercial Formulations of Risperidone for Treatment of Negative Symptoms of Schizophrenia

September 30, 2021

Company to Request Pre-NDA Meeting with U.S. Food and Drug Administration

WALTHAM, Mass., Sept. 30, 2021 (GLOBE NEWSWIRE) -- Minerva Neurosciences, Inc. (Nasdaq: NERV), a clinical-stage biopharmaceutical company focused on the development of therapies to treat central nervous system disorders, today announced results from a pivotal bioequivalence study comparing the risperidone formulations used in its late-stage Phase 2b and Phase 3 trials, and the planned commercial formulation. The study met all key pharmacokinetic (PK) objectives and the data demonstrate bioequivalence across the various formulations.

"The results demonstrate bioequivalence in terms of exposure between the formulations used in our two late-stage Phase 2b and Phase 3 efficacy and safety trials with risperidone and we believe that the data address certain FDA observations following the Company's Type C meeting in November 2020," said Dr. Remy Luthringer, Executive Chairman and Chief Executive Officer of Minerva. "These results represent important progress along Minerva's critical path toward submission of an NDA for risperidone for the treatment of negative symptoms of schizophrenia, for which there are currently no approved treatment options in the United States."

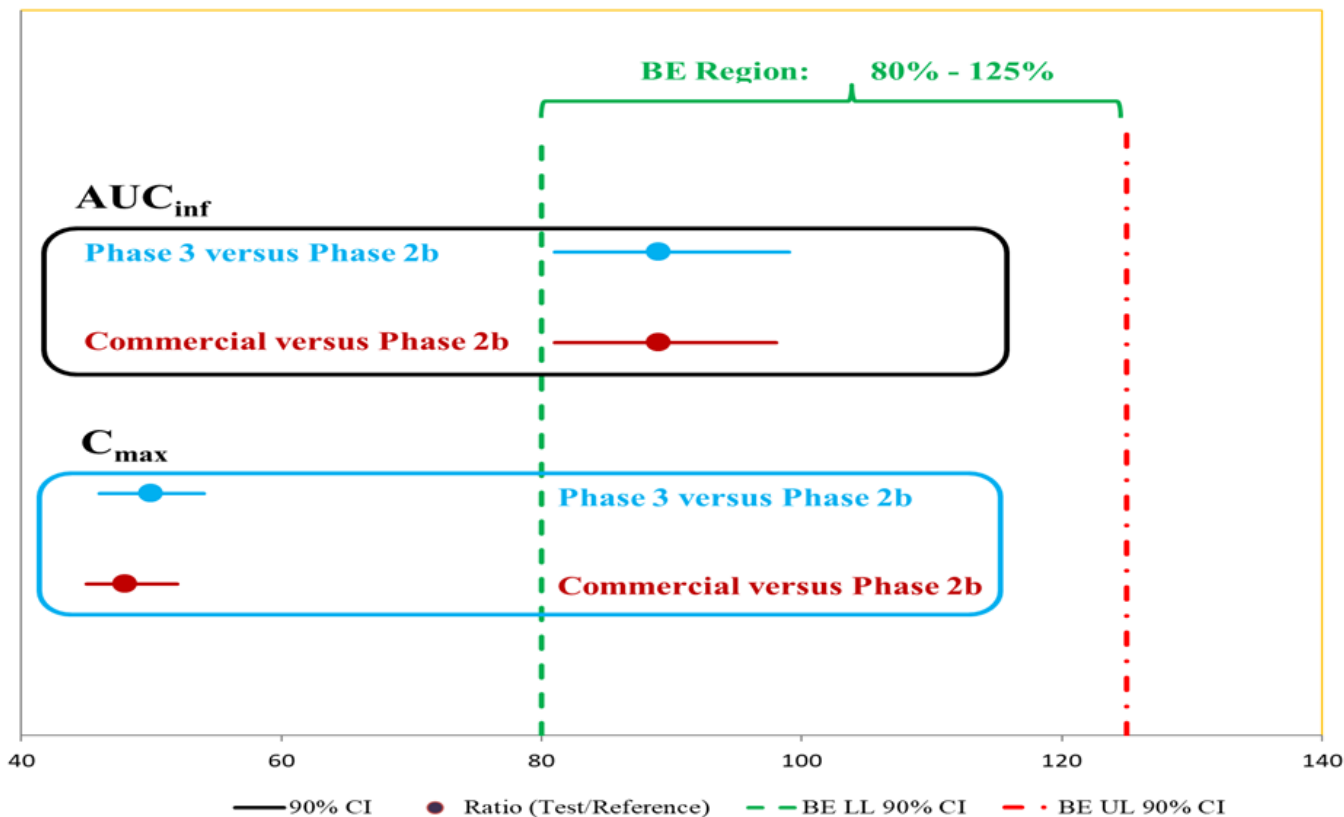
The area under the curve to last detectable concentration (AUC_{last}), the area under the curve extrapolated to infinity (AUC_{inf}), and the maximum plasma concentration (C_{max}) are the most commonly used plasma pharmacokinetic parameters to evaluate bioequivalence between various formulations.

For risperidone, efficacy is mostly driven by plasma exposure of the drug (i.e., AUCs) whereas safety margins improve by reducing C_{max} of the drug. Furthermore, as risperidone is intended for chronic use and the assessed formulations are controlled release, AUC_{inf} is the most relevant of the AUCs when single dose data are collected and used for determining bioequivalence.

In this study, the two most important objectives were to establish:

- The comparability under fasted condition of the 64 milligram (mg) tablet of the Phase 3 formulation of risperidone compared to the 64 mg dose based on the administration of two 32 mg tablets of risperidone used in the Phase 2b study, and
- The comparability under fasted condition of a 64 mg tablet of the planned commercial formulation of risperidone compared to the 64 mg dose based on the administration of two 32 mg tablets of risperidone used in the Phase 2b study.

As presented in Figure 1 for both objectives, the AUC_{inf} were bioequivalent, and the C_{max} of the reformulated phase 3 and planned commercial formulations were reduced substantially compared to the Phase 2b formulation.



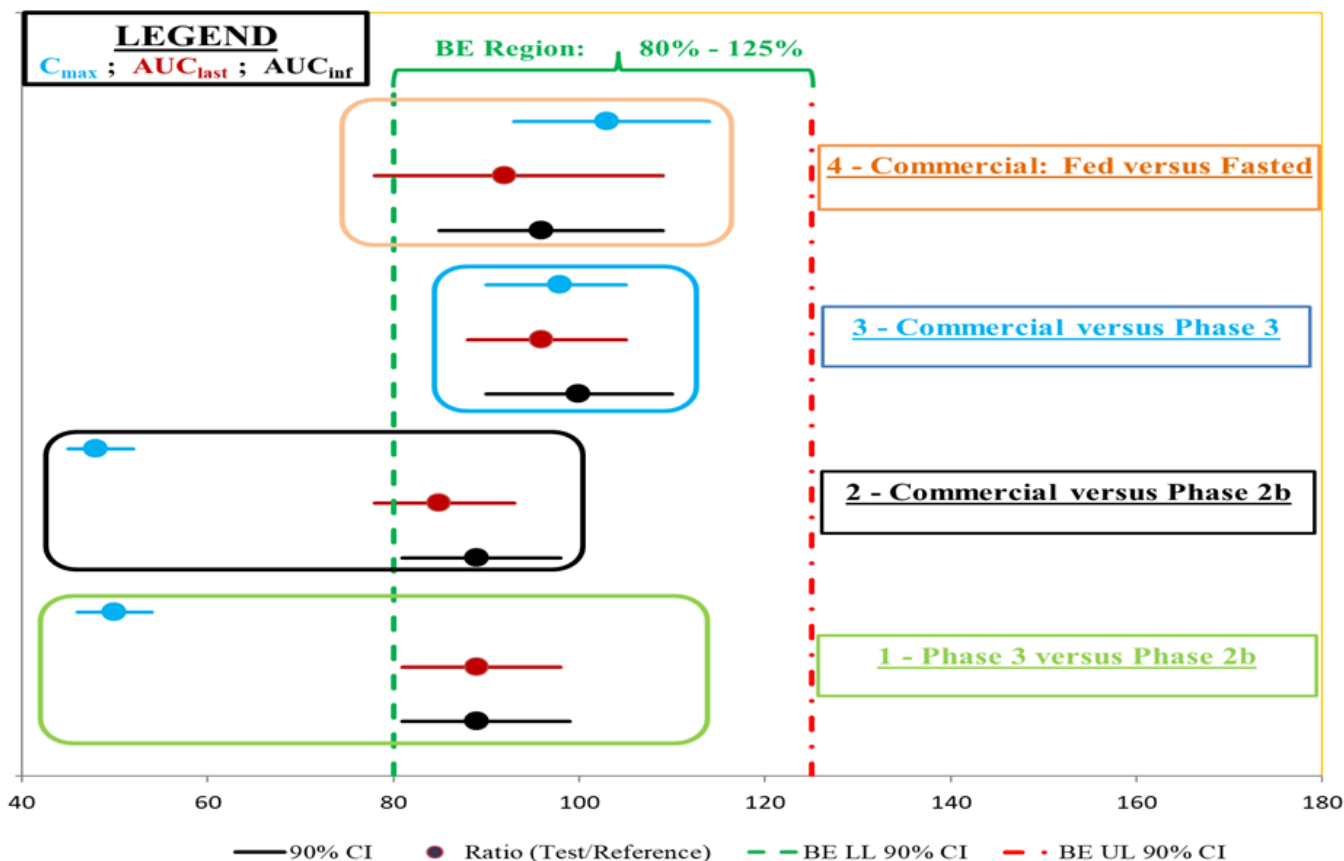
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Figure 1: Comparisons of AUC_{inf} and C_{max} between Phase 3 and phase 2b formulations, and planned commercial and Phase 2b formulations: 90% CI = 90% Confidence Interval; Ratio (Test/Reference); BE LL 90% CI = Bioequivalence Lower Level 90% Confidence Interval cutoff; BE UL 90% CI = Bioequivalence Upper Level 90% Confidence Interval cutoff

The additional two objectives of the study were to establish:

- The comparability under fasted condition of the 64 mg formulation of the planned commercial tablets compared to that used in the Phase 3 for which the results show bioequivalence between the formulations in terms of AUCs and C_{max} .
- and
- The comparability of the 64 mg dose of the commercial formulation under fed condition compared to fasted condition for which the results show bioequivalence of both AUC_{inf} and C_{max} between the fed and fasted conditions.

Figure 2 presents a summary of the four study objective results:



<https://www.globenewswire.com/NewsRoom/AttachmentNo/626c9e24-4fde-43f4-9196-c8e3e9220971>

Figure 2: The four study objectives are listed on the right across from the bioequivalence testing results for C_{max} , AUC_{last} , and AUC_{inf} . Other symbols are similar to those presented in Figure 1 above.

Dr. Luthringer added, "The additional results obtained are significant as they demonstrate the comparability of the formulations used in the late-stage efficacy and safety trials of roluperidone with the planned commercial formulation and allow administration of the drug with or without food. We intend to submit a request to the FDA for a pre-NDA meeting."

Study description:

Subject screening in this study was initiated on April 23, 2021, the completion of the enrollment of 48 healthy volunteers was announced on June 29, 2021, and the last subject assessment took place on July 26, 2021. Subjects were randomized to the four treatment sequences described above in a 1:1:1:1 ratio.

Of the 48 subjects randomized, 45 completed all study periods. Male subjects constituted 69% of the participants, and 75% of the subjects were white. Median age was 36 years, and all had negative SARS-CoV2 status at the beginning of the study and of every study period with the exception of 1 subject who tested positive at the beginning of study Period 4 and was discontinued. The mean body mass index was 28.1 ± 4 kg/m².

About Schizophrenia and Negative Symptoms

Schizophrenia is a chronic, severe and debilitating type of mental illness characterized by distortions in thinking, perception, emotions, language, sense of self and behavior. Schizophrenia affects 20 million people worldwide. ([World Health Organization](http://www.who.int)).

Negative symptoms can cause individuals with schizophrenia to withdraw from society, become disinterested or unable to complete tasks or feel pleasure. Negative symptoms are characterized by five constructs: blunted affect, avolition, anhedonia, and asociality ([Marder and Galderisi, 2017](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5411111/)).

Negative symptoms are the main cause of the poor functional outcome of patients suffering from schizophrenia ([Harvey et al., 2020](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC7011111/)) and may also be one of the main reasons ultrahigh risk adolescents may develop full blown schizophrenia ([Gomes and Grace, 2017](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC6911111/)). There are currently no treatments approved for negative symptoms of schizophrenia.

About Minerva Neurosciences

Minerva Neurosciences, Inc. (Nasdaq: NERV) is a clinical-stage biopharmaceutical company focused on developing product candidates to treat central nervous system (CNS) diseases. Our goal is to transform the lives of patients with improved therapeutic options. Minerva's portfolio of compounds includes roluperidone (MIN-101), in clinical development for negative symptoms of schizophrenia, and MIN-301, in pre-clinical development for Parkinson's disease. For more information, please visit our [website](http://www.minervaneurosciences.com).

Forward-Looking Safe Harbor Statement

This press release contains forward-looking statements. Forward-looking statements are statements that are not historical facts, reflect management's expectations as of the date of this press release, and involve certain risks and uncertainties. Forward-looking statements include, but are not limited to, statements herein with respect to the timing and scope of clinical trials and regulatory review and results and outcomes of such clinical trials, including the clinical development of roluperidone (MIN-101) for the treatment of negative symptoms of schizophrenia; the clinical and therapeutic potential of this compound, including its potential benefits in the treatment of negative symptoms of schizophrenia or any other indication; the timing and outcomes of future interactions with U.S. and foreign regulatory bodies, including the U.S. Food and Drug Administration; our ability to successfully develop and commercialize our therapeutic products; and management's ability to successfully achieve its goals. These forward-looking statements are based on our current expectations and may differ materially from actual results due to a variety of factors including, without limitation, the risk that trials and studies may be delayed and may not have satisfactory outcomes, the risk that initial or interim results from a clinical trial may not be predictive of the final results of the trial or the results of future trials, whether roluperidone will advance further in the clinical trials process and whether and when, if at all, it will receive final approval from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies and for which indications; whether any of our therapeutic products or setorexant will be successfully marketed if approved; whether any of our therapeutic product discovery and development efforts will be successful; management's ability to successfully achieve its goals; our ability to raise additional capital to fund our operations on terms acceptable to us; changes in expected or existing competition; unexpected litigation or other disputes; the impacts of the COVID-19 pandemic on our business; and general economic conditions. These and other potential risks and uncertainties that could cause actual results to differ from the results predicted are more fully detailed under the caption "Risk Factors" in our filings with the Securities and Exchange Commission, including our Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, filed with the Securities and Exchange Commission (SEC) on August 2, 2021. Copies of reports filed with the SEC are posted on our website at www.minervaneurosciences.com. The forward-looking statements in this press release are based on information available to us as of the date hereof, and we disclaim any obligation to update any forward-looking statements, except as required by law.

For more information:

Investor inquiries:

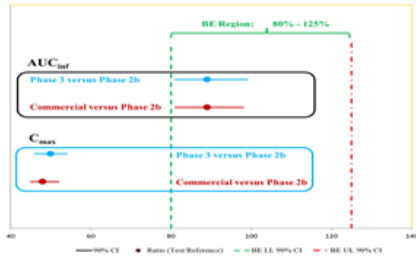
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Figure 1



Comparisons of AUCinf and Cmax between Phase 3 and phase 2b formulations, and planned commercial and Phase 2b formulations: 90% CI = 90% Confidence Interval; Ratio (Test/Reference); BE LL 90% CI = Bioequivalence Lower Level 90% Confidence Interval cutoff; BE UL 90% CI = Bioequivalence Upper Level 90% Confidence Interval cutoff

Figure 2

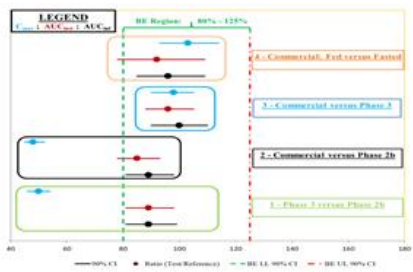


Figure 2: The four study objectives are listed on the right across from the bioequivalence testing results for C_{max} (●), AUC_{inf} (●), and AUC_{last} (●). Other symbols are similar to those presented in Figure 1 above.

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